Please amend the above-identified application as follows:

<u>In the Specification</u>:

Please replace the paragraph beginning at page 2, line 15 with the following rewritten paragraph:

--Accordingly, in accordance with the above objects, the present invention provides methods of detecting a target analyte in a test sample comprising a redox active molecule and an analyte. The method comprises applying an input signal to the test sample and detecting a change in the faradaic impedance of the system as a result of the association of the redox active molecule with the analyte.--

Please replace the paragraph beginning at page 2, line 25 with the following rewritten paragraph:

--The methods further comprise applying a first input signal to said redox active complex; the input signal can comprise an AC component and/or a DC component.--

Please insert the following paragraph beginning at line 9 on page 4 of the specification:

--Figures 7A-T depict the configurations of a number of specific systems according to the invention. Figure 7A depicts a system used to detect pollutants. Figures 7B-E depict systems used to detect target analytes that bind to a binding ligand specifically. Figure 7F depicts a system in which binding of a target analyte theoretically affects the H_{AB} between the RAM and the electrode. Figure 7G depicts a system similar to Figure 7F, except that the binding ligand is inherent in the attachment of the RAM to the electrode. Figure 7H depicts a situation in which the analyte also serves as the redox active

molecule. Figure 7I depicts a competitive-type assay which relies on a decrease in signal for detection. Figure 7J depicts a competitive-type assay which results in a change in signal, rather than a decrease in signal. Figure 7K depicts a system that utilizes a change in the diffusion coefficient upon analyte binding for the change in faradaic impedance and mass transfer. Figure 7L depicts a system that relies on a change in ligands to result in a change in E_0 of the system. Figure 7M is a variation of the previous system, and depicts a situation in which the RAM and the BL are closely associated or linked. Figure 7N depicts a system that results in changes in faradaic impedance as a result of changing E_0 or H_{AB}. Figure 7O depicts a system that uses two binding ligands, BL_1 and BL_2, which may be the same or different, to alter the environment of the RAM. Figure 7P depicts a system in which a target analyte is used that will bind the metal ion-binding ligand complex in such a way as to render the metal unavailable to serve as a redox active molecule. Figure 7Q depicts a system that utilizes a change in metal ion affinity to a particular binding ligand to detect a change in the signal based on a different metal being present (resulting in a different E_0). Figure 7R is a variation of the system shown in Figure 7I, and depicts a competitive-type assay for detecting a target analyte. Figure 7S is a mixture of Figure 7B and 7R, and depicts a system where the replacement of a bulky analog by a smaller target analyte results in a different signal. Figure 7T depicts a two electrode system in a competitive-type assay.--

Please replace the paragraph beginning at page 14, line 1 with the following rewritten paragraph:

--In a preferred embodiment, the system is used to detect pollutants, such as organic pollutants, as is depicted in System 1, Figure 7A.--

Serial No.: 09/096,593
Filed: June 12, 1998

Please delete the drawing at page 14, lines 3-8.

Please replace the paragraph beginning at page 14, line 24 with the following rewritten paragraph:

--Systems 2, 3, 4, and 5 (see figures 7B-7E, respectively) depict a similar situation except that a specific interaction is exploited. Thus, the target analyte will bind to the binding ligand specifically, and is generally large as compared to the binding ligand and RAM. Upon binding, the local environment of the RAM is affected, for example potentially by changing the E_0 of the RAM or the solvent reorganization energy, and thus results in a change in the faradaic impedance of the system in the presence of the analyte. The target analyte in these cases could be protein, a cell, etc. In addition, any or all of these systems may be used with co-redoxants, as described below. Upon binding of the target analyte, the access of the co-redoxant to the RAM is restricted, thus resulting in either a different signal or a loss in signal, or both. In addition, as for all the systems depicted herein, the order or proximity of the individual molecules of the monolayer is not determinative.--

Please delete the drawing at page 14, lines 34-39.

Please delete the drawings at page 15, lines 7-24.

Please replace the paragraph beginning at page 15, line 25 with the following rewritten paragraph:

--System 6 (see Figure 7F) depicts a system in which binding of a target analyte theoretically affects the HAB between the RAM and the electrode:--

Please delete the drawing at page 15, lines 27-33.

Please replace the paragraph beginning at page 15, line 34 with the following

rewritten paragraph:

--System 7 (see Figure 7G) depicts a similar situation, except that the binding ligand is inherent in the attachment of the RAM to the electrode; for example, it may be a peptide or nucleic acid to which the analyte binds.--

Please delete line 36 on page 15.

Please delete the drawing at page 16, lines 1-5.

Please replace the paragraph beginning at page 16, line 6 with the following rewritten paragraph:

--System 8 (see Figure 7H) depicts a situation in which the analyte also serves as the redox active molecule; this is particularly useful in the detection of metal ions, for example heavy metal ions, which are toxic. System 8 depicts a metal ion, M, and a metal ligand, ML, although as will be appreciated by those in the art, it is quite possible to have the analyte in this case be a metalloprotein, with a BL, etc. As will be appreciated by those in the art, System 8 is particularly useful in the detection of different metal ions, using an array of different ligands; preferential binding of one metal over another would result in a panel of results that can be correlated to metal ligand binding. Moreover, different metals may have different E_0s and thus give different signals.--

Please delete the drawing at page 16, lines 14-19.

Please replace the paragraph beginning at page 16, line 20 with the following rewritten paragraph:

--System 9 (see Figure 7I) depicts a competitive-type assay which relies on a decrease in signal for detection. In this case, the target analyte is a ligand, for example carbon monoxide (CO), which are stronger ligands (SMLs, i.e. have higher binding

constants) for a particular metal than the weaker metal ligand (WML) of the system.--

Please delete the drawing at page 16, lines 24-29.

Please replace the paragraph beginning at page 16, line 30 with the following rewritten paragraph:

--System 10 (see Figure7J) depicts a similar type of assay, which results in a change in signal rather than a decrease in signal. For example, E_0 and λ could both change as a result of a new ligand binding.--

Please delete the drawing at page 16, lines 32-39.

Please replace the paragraph beginning at page 17, line 1 with the following rewritten paragraph:

--System 11 (see Figure 7K) utilizes a change in the diffusion coefficient upon analyte binding for the change in faradaic impedance and mass transfer. In this embodiment, when the ligands are not covalently attached to an electrode, changes in the diffusion coefficient will alter the mass transfer impedance and thus the total faradaic impedance. That is, in some circumstances the frequency response of a redox active complex will be limited by its diffusion coefficient. Also, the charge transfer impedance may be altered by the binding of an analyte. At high frequencies, a redox active complex may not diffuse rapidly enough to reversibly transfer its electron to the electrode at a rate sufficient to generate a strong output signal. At low frequencies, the molecule has sufficient time to diffuse, and thus an output signal can be detected. In this embodiment, the use of monolayers is generally not preferred. –

Please delete the drawing at page 17, lines 22-27.

Please replace the paragraph at page 17, lines 28 with the following rewritten

paragraph:

--System 12 (see Figure 7L) is similar to systems 10 and 11, as it is a sensor for different ligands, but it relies on a change in ligands to result in a change in E_0 of the system. A similar system may be used with two metals; that is, instead of adding strong metal ligands, a different metal, with different affinity for the ligands may be added, resulting in a electrochemical change.--

Please delete the drawing at page 18, lines 1-6.

Please replace the paragraph beginning at page 18, line 7 with the following rewritten paragraph:

--System 13 (see Figure 7M) is a variation on previous systems, except that the RAM and the BL are closely associated or linked.--

Please delete the drawing at page 18, lines 9-14.

Please replace the paragraph beginning at page 18, line 15 with the following rewritten paragraph:

--System 14 (see Figure 7N) results in changes in faradaic impedance as a result of changes in E_0 or H_{AB}. In this case, the binding ligand will self-associate in some way, bringing the RAM into closer proximity to the electrode. For example, the binding ligand may be a nucleic acid (for example for the detection of a nucleic acid binding protein) or a protein (for example for the detection of proteins that inhibit or bind the binding ligand protein. Upon binding of the target, for example a protein, the conformation and thus the local environment of the RAM changes, resulting in a detectable signal. System 14 could also be run in "reverse", wherein the association of the analyte brings the RAM into proximity of the surface.--

Please delete the drawing at page 18, lines 23-28.

Please replace the paragraph beginning at page 18, line 29 with the following rewritten paragraph:

--System 15 (see Figure 7O) uses two binding ligands, BL1 and BL2, which may be the same or different, to alter the environment of the RAM. It may be desirable to have one of the binding ligands be a somewhat "generic" binding ligand. Changes in E_0 and/or impedance will result in a detectable signal.--

Please delete the drawing at page 18, lines 32-39.

Please replace the paragraph beginning at page 19, line 1 with the following rewritten paragraph:

--System 16 (see Figure 7P) also relies on a decrease in signal. In this embodiment, a target analyte is used that will bind the metal ion-binding ligand complex in such a way as to render the metal unavailable to serve as a redox active molecule.--

Please delete the drawing at page 19, lines 4-8.

Please replace the paragraph beginning at page 19, line 9 with the following rewritten paragraph:

--System 17 (see Figure 7Q) utilizes a change in metal ion affinity to a particular binding ligand to detect a change in the signal based on a different metal being present (resulting in a different E_0).--

Please delete the drawing at page 19, lines 11-16.

Please replace the paragraph beginning at page 19, line 17 with the following rewritten paragraph:

--System 18 (see Figure 7R) is similar to System 9 and depicts a competitive-

type assay for detecting a target analyte. In System 18, a covalently attached target analyte or target analog (TA) is competed off the binding ligand by the addition of the target analyte, resulting in a decrease in signal.--

Please delete the drawing at page 19, lines 20-25.

Please replace the paragraph beginning at page 19, line 26 with the following rewritten paragraph:

--System 19 (see Figure 7S) is a mixture of Systems 2 and 18, where the replacement of a bulky analog (TA) by a smaller target analyte (T) results in a different signal. For example, co-redoxant reactions could now occur. Alternatively, monolayers with "holes", that would allow current flow in the absence of the analog but do not in its presence, could also be used.--

Please delete the drawing at page 19, lines 30-35.

Please replace the paragraph at page 20, line 1 with the following rewritten paragraph:

--System 20 (see Figure 7T) depicts a two electrode system in a competitive-type assay. This is useful in that it allows detection of an increase in signal on the second electrode, which is generally preferable to the loss of a signal. –

Please delete the drawing at page 20, lines 4-15.

Please replace the paragraph beginning at page 26, line 26 with the following rewritten paragraph:

--As will be appreciated by those in the art, a large number of possible conductive oligomers may be utilized. These include conductive oligomers falling within the Structure 1 and Structure 8 formulas, as well as other conductive oligomers, as are